EXHIBIT 25

Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Current policy effective date: 7/1/12
(See policy history boxes for previous effective dates)

Title: Pelvic Organ Prolapse Repair Using Synthetic Mesh

Description / Background

Pelvic organ prolapse (POP) is a medical condition that occurs when the normal support of the vagina is lost, resulting in "sagging" or dropping of the bladder, urethra, cervix and rectum. As the prolapse of the vagina and uterus progresses, women may feel bulging tissue protruding through the opening of the vagina. POP may be caused by a variety of factors including the effects of pregnancy, vaginal delivery or obesity. This quality of life issue for women becomes more prevalent with age. Types of POP include

- Anterior vaginal prolapse (also known as cystocele)
- Posterior vaginal prolapse (also known as rectocele)
- Uterine prolapse
- Vaginal prolapse after hysterectomy
- Rectal prolapse

Many conservative treatment options are available to treat POP, including dietary changes, pelvic floor muscle exercises, physical therapy and pessary use. One treatment for pelvic organ prolapse is a device inserted into the vagina called a pessary. Some women are so bothered by the symptoms resulting from their pelvic organ prolapse that they opt to have surgical repair.

Conventional surgical intervention for POP of the anterior vaginal wall includes laparoscopic anterior colporrhaphy and cystocele repair. In an anterior colporrhaphy, an incision is made in the front wall of the vagina. The vaginal skin is separated from the bladder wall behind it. The weak or frayed edges of the deep vaginal wall are found and the strong tissue next to edges are sutured to each other lifting the bladder and recreating the strong "wall" underneath it. The vaginal incision is then closed with dissolving stitches.

During laparoscopic repair of a cystocele any paravaginal defects are detected by the surgeon and repaired with several interrupted sutures with permanent stitches. Three different types of paravaginal defects exist that can be identified through the laparoscope, and each defect should be treated differently according to its own type of defect.

Surgical cystocele repair is very effective for most women. However, recurrent prolapse occurs in 25 to 30% of patients with a previous surgical repair. To reduce this recurrence of prolapse, a surgeon may choose to place a mesh graft material over the repair line to reinforce the repair. Studies are in progress to determine whether or not using grafts provides superior results when compared to traditional surgeries. The studies will also compare the risks of the two types of procedures and who benefits most from the mesh reinforcements.

There are several types of mesh repair systems available. They include, but are not limited to:

- Pelvitex™ Transvaginal Mesh (C. R. Bard) FDA approved in
- Perigee™ and Apogee™ (AMS)
- Avaulta™ (Bard)
- Prolift™ (Ethicon Gynecare)

In 1996, the United States Food and Drug Administration (FDA) approved polypropylene transvaginal mesh for the treatment of stress urinary incontinence. The mesh was approved to treat pelvic organ prolapse in 2002.

In October 2008, the FDA issued a public health notification to warn of serious complications related to the implantation of transvaginal mesh to treat pelvic prolapse and stress urinary incontinence. During the three years prior to that warning, the FDA had received more than 1,000 reports of complications related to vaginal mesh produced by nine manufacturers. The FDA reported that in 2010, approximately 300,000 women had transvaginal surgery to correct pelvic prolapse, while nearly 260,000 had transvaginal surgery for stress urinary incontinence. In both situations, a large percentage of these surgeries used mesh.

The FDA's literature review found that erosion of mesh through the vagina is the most common and consistently reported mesh-related complication from transvaginal POP surgeries using mesh. Mesh erosion can cause serious infections and can require multiple surgeries to repair and can be debilitating for some women. In some cases, even multiple surgeries will not resolve the complication. Mesh contraction (shrinkage) is a previously unidentified risk of transvaginal POP repair with mesh that has been reported in the published scientific literature and in adverse event reports to the FDA since the Oct. 20, 2008 FDA Public Health Notification. Reports in the literature associate mesh contraction with vaginal shortening, vaginal tightening, dyspareunia and severe pelvic pain.

In July 2011, the FDA issued another warning to physicians about the serious risks of this polypropylene mesh and clarified that traditional, non-polypropylene devices/mesh should be the primary course of treatment for pelvic organ prolapse. However, the FDA did not choose to have the polypropylene mesh repair systems pulled from the market. Initially, these devices were classified as Class II devices, meaning that FDA General Controls are not sufficient to assure safety and effectiveness and existing methods/standards/guidance documents are available to provide assurances of safety and effectiveness. Most Class II devices are approved via the 510K approval process. Going forward, however, any new mesh products to treat POP will be classified as Class III devices. Class III medical devices have the most stringent regulatory controls. For Class III medical devices, sufficient information is not available to assure safety and effectiveness through the application of General Controls and Special Controls.

When factoring in anatomic success, patient-oriented improvement and satisfaction and total reoperation rates, the success rates of native tissue repairs (without mesh) may be higher than

previously thought. The risk/benefit ratio for mesh-augmented vaginal repairs must balance improved anatomic support of the anterior vaginal wall against the cost of the devices and increased complications such as mesh erosion, exposure or extrusion, pelvic pain, groin pain and dyspareunia.

Pelvic organ prolapse repair using synthetic mesh remains a viable surgical option for specified patients when done by a physician specifically trained in this technique. Patients should be advised, prior to surgery, of the risks and possible complications of the procedure as stated by the FDA. Patients need to be counseled that there are alternative native tissue repairs and that synthetic mesh is permanent. Some post-op patients (who had the mesh inserted) may not realize that vaginal bleeding, pain and dyspareunia may be related to vaginal mesh, and such reports should prompt a thorough vaginal examination, and an examination under anesthesia if needed.

CPT / HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

C1781 57267

Other codes (investigational, not medically necessary, etc.):

N/A

Medical Policy Statement

The relative safety and effectiveness of the pelvic organ prolapse repair using synthetic mesh have been established. It may be considered a useful therapeutic option when indicated in carefully selected patients who have been thoroughly advised of possible risks and complications of the procedure.

Rationale

Altman et al. in 2012 reported on a study regarding outcomes of anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse. In this multicenter, parallel-group, randomized, controlled trial, the authors compared the use of a trocar-guided, transvaginal polypropylene-mesh repair kit with traditional colporrhaphy in women with prolapse of the anterior vaginal wall (cystocele). The primary outcome was a composite of the objective anatomical designation of stage 0 (no prolapse) or 1 (position of the anterior vaginal wall more than 1 cm above the hymen), according to the Pelvic Organ Prolapse Quantification system, and the subjective absence of symptoms of vaginal bulging 12 months after the surgery.

Of 389 women who were randomly assigned to a study treatment, 200 underwent prolapse repair with the transvaginal mesh kit and 189 underwent traditional colporrhaphy. At 1 year, the primary outcome was significantly more common in the women treated with transvaginal mesh repair (60.8%) than in those who underwent colporrhaphy (34.5%) absolute difference, 26.3 percentage points; 95% confidence interval, 15.6 to 37.0). The surgery lasted longer and the rates of intraoperative hemorrhage were higher in the mesh-repair group than in the

colporrhaphy group (P<0.001 for both comparisons). Rates of bladder perforation were 3.5% in the mesh-repair group and 0.5% in the colporrhaphy group (P = 0.07), and the respective rates of new stress urinary incontinence after surgery were 12.3% and 6.3% (P = 0.05). Surgical re-intervention to correct mesh exposure during follow-up occurred in 3.2% of 186 patients in the mesh-repair group.

The conclusion of this study indicated that, as compared with anterior colporrhaphy, use of a standardized, trocar-guided mesh kit for cystocele repair resulted in higher short-term rates of successful treatment but also in higher rates of surgical complications and postoperative adverse events.

In 2011, an article by Walter et al. provided an update on transvaginal mesh procedures, newly available minimally invasive surgical techniques for pelvic floor repair. A compilation of systematic reviews, randomized control trials/controlled clinical trials and observational studies were studied. The conclusion reached was that counseling for the surgical treatment of pelvic organ prolapse should consider all benefits, harms and costs of the surgical procedure, with particular emphasis on the use of mesh. The following recommendations were made:

1. Patients should be counseled that transvaginal mesh procedures are considered novel techniques for pelvic floor repair that demonstrate high rates of anatomical cure in uncontrolled short-term case series.
2. Patients should be informed of the range of success rates until stronger evidence of superiority is published.
3. Training specific to transvaginal mesh procedures should be undertaken before procedures are performed.
4. Patients should undergo thorough preoperative counseling regarding (a) the potential serious adverse sequelae of transvaginal mesh repairs, including mesh exposure, pain, and dyspareunia; and (b) the limited data available comparing transvaginal mesh systems with h traditional vaginal prolapse repairs or with traditional use of graft material in the form of augmented colporrhaphy and sacral colpopexy.

In 2010, Nieminen et al reported on a study of 202 women with anterior prolapse who were assigned to either have colporrhaphy alone or reinforced with a tailored polypropylene mesh. Before and 2, 12, 24 and 36 months after surgery the outcome was assessed by examination and standard questions. The primary endpoint was the recurrence of anterior vaginal prolapse. Secondary outcomes were symptom resolution, reoperation and mesh exposure.

Conclusion: At the 3 year follow-up, anterior colporrhaphy with mesh reinforcement significantly reduced anatomic recurrences of anterior vaginal prolapse, but no difference in symptomatic recurrence were noted and mesh erosion rate was high. The use of mesh was not associated with dyspareunia.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

Related Policies

N/A

Medicare Information

There is no national or local Medicare policy for this service.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

References

1. ICS (International Continence Society) 2005 Scientific Programme, ". Cystocele Repair Utilizing Anterior Wall Mesh Graft Placed via Double Trans-Obturator Approach (Perigee™ System), Page 595, 8/31/2005.
2. ACOG committee opinion: http://www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Gynecologic_Practice/Vaginal_Placement_of_Synthetic_Mesh_for_Pelvic_Organ_Prolapse (accessed 3/9/12)
3. Altman d, Vavrynen T, Engh ME, Axelsen S, Falconer C. Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011;364:1826-36.
4. American Urological Society Position Statement on the Use of Vaginal Mesh for the Surgical Repair of Stress Urinary Incontinence, available at http://www.auanet.org/content/aua-policies/position-statements/stress-urinary-incontinence.cfm (accessed 3/9/12).
5. American Urological Society Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Pelvic Organ Prolapse, available at http://www.auanet.org/content/aua-policies/position-statements/stress-urinary-incontinence.cfm (accessed 3/9/12)
6. AMS overview of Perigee system, available at < http://www.americanmedicalsystems.com/prof_product_detail_objectname_prof_female_perigee.html Perigee™ Transobturator Anterior Prolapse Repair System >, accessed 1/243/9/12.
7. AMS reimbursement guidelines for Perigee, available at < http://www.auanet.org/content/aua-policies/position-statements/stress-urinary-incontinence.cfmhttp://www.americanmedicalsystems.com/DAM_public/1000832r1-AMS-C-Codes-HCPCS-Crosswalk.pdf >, accessed 1/14/12.
8. Apogee/Perigee Clinical Study Summary. Available at < http://www.gsuelopelvico.com/extras/biblio/Apogee%20+%20Perigee%20Clinical%20Study%20Summary.pdf > (Accessed 3/9/12).
9. Baessler K. Do we need meshes in pelvic floor reconstruction. World J Urol. 2011 Nov 16. [Epub ahead of print]
10. Centers for Medicare and Medicaid Services (CMS), Medicare approval letter for clinical trials of Perigee™ System, June 14, 2005. Available at http://clinicaltrials.gov/ct2/show/results/NCT00535301 (accessed 3/9/12).
11. FDA 510K premarket approval, Perigee, available at < http://www.510kdecisions.com/applications/index.cfm/id/K081710/index.cfm >, accessed 1/24/12.
12. FDA executive summary. Surgical mesh for treatment of women with pelvic organ prolapse and stress urinary incontinence. Available at < http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalD

evices/MedicalDevicesAdvisoryCommittee/ObstetricsandGynecologyDevices/UCM270402.pdf .>, accessed 3/9/12.
13. ICS (International Continence Society) 2005 Scientific Programme, “A New Option in the Treatment of Pelvic Organ Prolapse (POP) (Transobturator Anterior Prolapse Repair System),” Page 607, 8/31/2005.
14. Ismail S. Complications of mesh kits for pelvic organ prolapse: a review of manufacturer and user facility device experience (MAUDE) databases. Available at < http://www.icsoffice.org/Abstracts/Publish/47/000009.pdf > (Accessed 3/9/12).
15. Jeffrey S and de Jong P. Mesh, grafts and kits in pelvic organ prolapse surgery: Where are we now? SAUGR V6N1 text 3/3/09. Available at < http://uct.academia.edu/StephenJeffery/Papers/101019/MESH_GRAFTS_AND_KITS_IN_PELVIC_ORGAN_PROLAPSE_SURGERY_WHERE_ARE_WE_NOW > (Accessed 3/9/12).
16. Lazarou G, Stohbehn K et al. Pelvic organ prolapse and management. Medscape Reference © 2011 WebMD, LLC, available at < http://emedicine.medscape.com/article/276259-treatment#a28 >, accessed 1/243/9/12.
17. Menefee SA, Dyer KY, Lukacz ES, Simsiman AJ, Luber KM, Nguyen JN. Colporrhaphy compared with mesh or graft-reinforced vaginal paravaginal repair for anterior vaginal wall prolapse: a randomized controlled trial. Obstet Gynecol. 2011 Dec;118(6):1337-44.
18. Nguyen JN, Burchette RJ. Outcome after anterior vaginal prolapse repair: a randomized controlled trial. Obstet Gynecol 2008 Apr;111(4):891-8.
19. Nguyen JN, Jakus-Waldman SM, Walter AJ, White T, Menefee SA. Perioperative complications and reoperations after incontinence and prolapse surgeries using prosthetic implants. Obstet Gynecol. 2012 Mar;119(3):539-46.
20. Nieminen K, Hiltunen R, Takala T, Heiskanen E, Merikari M, Niemi K, Heinonen PK. Outcomes after anterior vaginal wall repair with mesh: a randomized, controlled trial with a 3 year follow-up. Am J Obstet Gynecol. 2010 Sep;203(3):235.e1-8. Epub 2010 May 21.
21. Walter JE et al. Transvaginal Mesh Procedures for Pelvic Organ Prolapse. J Obstet Gynaecol Can 2011;33(2):168-174.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 3/9/12, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
12/9/05	12/9/05	12/9/05	Joint policy established
7/1/12	5/15/12	5/15/12	Policy title changed from "Perigee™ Transobturator Anterior Vaginal Prolapse Repair System" to "Pelvic Organ Prolapse Repair Using Synthetic Mesh." Policy status changed to "established" from experimental and investigational. Language added regarding possible complications from mesh insertion.

Next review: 2nd Qtr, 2013

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN: N/A	Revised: N/A
BCBSM: N/A	Revised: N/A

BLUE CARE NETWORK

POLICY: PELVIC ORGAN PROLAPSE REPAIR USING SYNTHETIC MESH

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered.
BCNA (Medicare Advantage)	Covered
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.
Blue Cross Complete of Michigan	Covered

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Appropriate copayments will apply.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.
- Payment is based on BCN payment rules, individual certificate benefits and certificate riders.